DETAILED ACTION

Applicants amendments and arguments filed 2/8/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously, applicants elected with traverse Group I. Since the species was unclear, in an interview (see 4/15/08) it was agreed that the species examined would be the peptide INSL3 (SEQ ID NO:7) as recited in claims 1 and 3 (i.e. no conjugate). As noted in the first office action (4/15/08) art was found that read on the elected species. The claims have been amended to read on species other than SEQ ID NO:7. Section 803.02 of the MPEP states: 'Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The **>examination< will be extended to the extent necessary to determine patentability of the Markush-type claim.' In the instant case, previously cited art reads on claim 1. In accord with section 803.02 of the MPEP, the examination was previously extended to the extent necessary to determine patentability of the Markush-type claim. Newly added claims 53-54 do not read on the originally elected species since SEQ ID NO:7 is distinct from the sequences recited in claims 53-54.

Claims 2,5-6,9,24-31,34-49 have been cancelled.

Claims 4,7-8,10-23,50-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/13/08.

Claims 1,3,32-33 are under consideration.

Claim Rejections - 35 USC § 112

Claism were previously rejected under 112 2nd. Since the claims have been amended the rejection is updated.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3,32-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Previously, claim 1 and dependent claims were drawn to 'analogues'. Currently the claims are drawn to peptides that have modifications. Claim 3 expressly states that the peptide is modified from a particular sequence. However, the scope of the modifications are unclear. In particular, it is unclear where the modifications are located. As such, the metes and bounds of the claims are unclear.

In the instant case, the claims recite wherein clauses. However, the wherein clauses do not set forth the structural features of the peptides. The instant claims refer to positions 2 and 8 and positions 21 and 26 of 'said peptide sequences'. However, the claims refer to 'synthetic monomeric, cyclic B-chain peptide' as well as SEQ ID NO:1 for example. Since SEQ ID NO:1 is not cyclic the 'synthetic monomeric, cyclic B-chain peptide' is not the equivalent of SEQ ID NO:1. It is unclear if 'said peptide sequences' is in reference to the cyclic (or modified) peptide

or if 'said peptide sequences' is in reference to specific SEQ ID NOs. It is noted that if the reference is to the cyclic (or modified) peptide it is unclear if the cyclic portion is numbered and counted clockwise or counterclockwise.

Section 2111 of the MPEP states that claims are to be given the broadest reasonable interpretation consistent with the specification. It is noted that claim 1 and 3 refer to SEQ ID NO:7 which is a 31 amino acid sequence: PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. The specification (Figure 3, and dependent claims 50-51) teach particular peptides that are apparently based on SEQ ID NO:7. The claims refer to modifications within the range of positions 2 to 8 and 21 to 26. The peptide identified as cINSL3a (see figure 3 and claim 50) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), positions 29-31 (deletion of TEA) if one were to interpret the modifications in relation to SEQ ID NO:7. Thus, there are modification outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. It would not be consistent with the specification to interpret positions 2 and 8, and positions 21 and 26 as in reference to SEQ ID NO:7. It is noted that if the reference is to the cyclic (or modified) peptide it is unclear if the cyclic portion is numbered and counted clockwise or counterclockwise. Further, since the claims allow spacer groups it is unclear how such groups would alter the numbering. Further, the peptide identified as cINSL3b (see figure 3 and claim 51) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), position 12 (change of H to R), positions 29-31 (deletion of TEA) in relation to SEQ ID NO:7. Thus, there are at least 6 modifications outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ

ID NO:7 as the peptide basis of comparison. As claimed, it is unclear where modifications are permissible.

Although unclear, for purposes of examination the claims have been interpreted such that the peptides are cyclic. Since the location of the cyclic modification is unclear, any cyclic modification is interpreted as reading on the claims. Further, the claims have been interpreted such that the cyclic peptide must have one residue in common with the recited SEQ IDs and other modifications can occur at any other position.

Response to Arguments 112 2nd

Since the claims have been amended, a rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (pages 8-11) that the word modified as used in claim 3 are the same modifications of claim 1.

Applicants argue that a skilled artisan would understand that the numbering is such that the positions are numbered left to right and refer to Figure 3.

Applicant's arguments filed 2/8/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 8-11) that the word modified as used in claim 3 are the same modifications of claim 1, from the claim it is unclear where modifications are permissible. Further, it is unclear how the amino acid positions are being numbered. If the modifications and numbering are unclear in claim 1 then the modifications and numbering of claim 3 are also unclear. Section 2111 of the MPEP states that claims are to be given the broadest reasonable

interpretation consistent with the specification. First, it is noted that claim 1 refers to SEQ ID NOs. However, the claims state that there are modifications. Thus the claims refer to unmodified and modified peptides. It is noted that SEQ ID NO:7, for example, is separate and distinct from modified SEQ ID NO:7. The specification (page 5 line 14) refers to at least two modifications. Page 14 of the specification refers to various modifications. As claimed, it is unclear where the modifications may occur. It is noted that claim 1 and 3 refer to SEQ ID NO:7 which is a 31 amino acid sequence: PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. The specification (Figure 3, and dependent claims 50-51) teach particular peptides that are apparently based on SEQ ID NO:7. The claims refer to modifications within the range of positions 2 to 8 and 21 to 26. The peptide identified as cINSL3a (see figure 3 and claim 50) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), positions 29-31 (deletion of TEA) if one were to interpret the modifications in relation to SEQ ID NO:7. Thus, there are modification outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. It would not be consistent with the specification to interpret positions 2 and 8, and positions 21 and 26 as in reference to SEQ ID NO:7. It is noted that if the reference is to the cyclic (or modified) peptide it is unclear if the cyclic portion is numbered and counted clockwise or counterclockwise. Further, since the claims allow spacer groups it is unclear how such groups would alter the numbering. Further, the peptide identified as cINSL3b (see figure 3 and claim 51) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), position 12 (change of H to R), positions 29-31 (deletion of TEA) in relation to SEQ ID NO:7. Thus, there are at least 6 modifications outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID

NO:7 as the peptide basis of comparison. As claimed, it is unclear where modifications are permissible.

Although Applicants argue that a skilled artisan would understand that the numbering is such that the positions are numbered left to right and refer to Figure 3, the claims merely refer to 'of said peptide sequences'. The claims refer to both cyclic peptides and peptides of particular SEQ IDs. The claims recite that spacer groups can be present. It is noted that Glycine residues are often used as spacer groups. Upon insertion of Glycine residues, the numbering system is unclear. As discussed above, if the particular SEQ IDs are used in the numbering scheme as argued by the applicant there are modifications outside of positions 2 and 8, and 21 and 26. The peptide identified as cINSL3b (see figure 3 and claim 51) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), position 12 (change of H to R), positions 29-31 (deletion of TEA) in relation to SEQ ID NO:7. Thus, there are at least 6 modifications outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. Thus, using the numbering system as argued by the applicant is inconsistent with the instant specification. Applicants argue that the claims imply modifications at positions 2 and 8, and 21 and 26 related to SEQ ID NO:7 (see claim 3). However, applicants own dependent claims (see claims 50-51) show modifications outside that range. The peptide identified as cINSL3b (see figure 3 and claim 51) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), position 12 (change of H to R), positions 29-31 (deletion of TEA) in relation to SEQ ID NO:7.

Previously, claims were rejected under 112 1st written description. Since claims have been amended an updated rejection appears below.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3,32-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus …") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of

such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to peptides. Claim 3 states that the analogue is modified from a sequence set forth in SEQ ID NO:7 Although unclear, for purposes of examination the claims have been interpreted such that the peptides are cyclic. Since the location of the cyclic modification is unclear, any cyclic modification is interpreted as reading on the claims. Further, the claims have been interpreted such that the cyclic peptide must have one residue in common with the recited SEQ IDs and other modifications can occur at any other position.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high. However, the ability to predict any and all sequences that bind to a biological target of the relaxin superfamily protein and modulate an activity of the biological target is limited.

(2) Partial structure:

In the instant case, the claims are drawn to peptides. Claim 3 states that the peptide is modified from a sequence set forth in SEQ ID NO:7 Although unclear, for purposes of examination the claims have been interpreted such that the peptides are cyclic. Since the location of the cyclic modification is unclear, any cyclic modification is interpreted as reading on the claims. Further, the claims have been interpreted such that the cyclic peptide must have one

residue in common with the recited SEQ IDs and other modifications can occur at any other position. It is noted that claim 1 and 3 refer to SEQ ID NO:7 which is a 31 amino acid sequence: PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. The specification (Figure 3, and dependent claims 50-51) teach particular peptides that are apparently based on SEQ ID NO:7. The claims refer to modifications within the range of positions 2 to 8 and 21 to 26. The peptide identified as cINSL3a (see figure 3 and claim 50) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), positions 29-31 (deletion of TEA) if one were to interpret the modifications in relation to SEQ ID NO:7. Thus, there are modification outside of the recited range of positions 2 and 8 and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. Further, the peptide identified as cINSL3b (see figure 3 and claim 51) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), position 12 (change of H to R), positions 29-31 (deletion of TEA) in relation to SEQ ID NO:7. Thus, there are at least 6 modifications outside of the recited range of positions 2 and 8 and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. Thus, consistent with the specification as long as a cyclic modification is present any amount of other modifications or substitutions is permissible.

In considering the possible variability, if SEQ ID NO:7 (31 amino acids) was substituted at every position except for the cysteine residues with any of the 20 natural amino acids (i.e. an analog) there would be 20^{29} (i.e. 536870912000000000000000000000000000) possible analogues. If there are substitutions with alkylmalonyl groups as discussed in section 0072 or if fusion compounds are considered the variability further increases. Hence, there is substantial variability in the genus.

Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over 20^{29} possible peptides). Further, it is noted that the examples are not necessarily representative of the instant genus. SEQ ID NO:2 is 29 amino acids in length while cRlx of Figure 3 is 25 amino acids in length. SEQ ID NO:2 includes a Cys at position 11 and 23 while cRLx includes a Ser at such positions. The instant claims do not specifically reflect the substitution of Cys for Ser and the deletion of amino acids. SEQ ID NO:7 is 31 amino acids in length while cINSL3b is 27 amino acids in length. SEQ ID NO:7 includes a Cys at positions 10 and 22 and a His at position 12 which are not present in cINSL3b. Further, the instant claims refer to modifications at positions within a range of 2 and 8 and 21 and 26 that include thioethers and spacer groups. The examples merely show linkages from positions 2-3 and disulfide bonds. There appear to be no examples based on SEQ ID NO:8-9 for example.

Since there are a substantial variety of peptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

Claim 1 states that the peptides bind a biological target of the relaxin superfamily protein and modulate an activity of the biological target.

However, there is no disclosed correlation between structure and function for all of the peptides. It is noted that claim 3 recites a particular sequence but the claim is drawn to a peptide modified from that sequence. As such, there is no common core sequence. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability

to bind a biological target. Although the claims refer to cross-links between positions 2 and 8 and 21 and 26 there is no teaching for the different sequences relating to the function of such residues. In particular, no common core sequence is taught. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention:

The specification (specifically example 1) describes the solid-phase synthesis of peptides, however the specification fail to describe the synthesis of a representative number of peptides. Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over 20^{29} possible analogues). Further, it is noted that the examples are not necessarily representative of the instant genus. SEQ ID NO:2 is 29 amino acids in length while cRlx of Figure 3 is 25 amino acids in length. SEQ ID NO:2 includes a Cys at position 11 and 23 while cRLx includes a Ser at such positions. The instant claims do not specifically reflect the substitution of Cys for Ser and the deletion of amino acids. SEQ ID NO:7 is 31 amino acids in length while cINSL3b is 27 amino acids in length. SEQ ID NO:7 includes a Cys at positions 10 and 22 and a His at position 12 which are not present in cINSL3b. Further, the instant claims refer to modifications at positions within a range of 2 and 8 and 21 and 26 that include thioethers and spacer groups. The examples merely show linkages from positions 2-3 and disulfide bonds.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1,3,32-33 is/are broad and generic, with respect to all possible peptides encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the peptides beyond those peptides specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of peptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of peptides embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Arguments 112 written description

Since the claims have been amended, a rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (pages 11-13) that the claims recite modifications of merely 7 discrete starting molecules.

Applicants argue that the clams recite a conformational constraint.

Applicants argue that Figure 3 provides examples of cyclic peptides

Applicants argue that the peptides as claimed bind to a biological target.

Applicant's arguments filed 2/8/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 11-13) that the claims recite modifications of merely 7 discrete starting molecules, the instant claims are not drawn to the molecules themselves but to modifications of the molecules. It is noted that claim 1 and 3 refer to SEQ ID NO:7 which is a 31 amino acid sequence: PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. The specification (Figure 3, and dependent claims 50-51) teach particular peptides that are apparently based on SEQ ID NO:7. The claims refer to modifications within the range of positions 2 to 8 and 21 to 26. The peptide identified as cINSL3a (see figure 3 and claim 50) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), positions 29-31 (deletion of TEA) if one were to interpret the modifications in relation to SEQ ID NO:7. Thus, there are modification outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. Further, the peptide identified as cINSL3b (see figure 3 and claim 51) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), position 12 (change of H to R), positions 29-31 (deletion of TEA) in relation to SEQ ID NO:7. Thus, there are at least 6 modifications outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison.

Thus, consistent with the specification as long as a cyclic modification is present any amount of other modifications, substitutions is permissible.

Although Applicants argue that the clams recite a conformational constraint, a conformational constraint is not a significant partial structure. In considering the possible variability, if SEQ ID NO:7 (31 amino acids) was substituted at every position except for the cysteine residues with any of the 20 natural amino acids (i.e. an analog) there would be 20^{29} (i.e. 536870912000000000000000000000000000) possible analogues.

Although Applicants argue that Figure 3 provides examples of cyclic peptides, in considering the possible variability, if SEQ ID NO:7 (31 amino acids) was substituted at every position except for the cysteine residues with any of the 20 natural amino acids (i.e. an analog) there would be 20^{29} (i.e. 536870912000000000000000000000000000) possible analogues. Figure 3 shows 3 cyclic peptides (SEQ ID NOs: 11-13). However, the 3 examples provided are not representative of the genus (which includes well over 20^{29} possible peptides). Further, it is noted that the examples are not necessarily representative of the instant genus. SEQ ID NO:2 is 29 amino acids in length while cRlx of Figure 3 is 25 amino acids in length. SEQ ID NO:2 includes a Cys at position 11 and 23 while cRLx includes a Ser at such positions. The instant claims do not specifically reflect the substitution of Cys for Ser and the deletion of amino acids. SEQ ID NO:7 is 31 amino acids in length while cINSL3b is 27 amino acids in length. SEQ ID NO:7 includes a Cys at positions 10 and 22 and a His at position 12 which are not present in cINSL3b. Further, the instant claims refer to modifications at positions within a range of 2 and 8 and 21 and 26 that include thioethers and spacer groups. The examples merely show linkages

from positions 2-3 and disulfide bonds. There appear to be no examples based on SEQ ID NO:8-9 for example.

Although Applicants argue that the peptides as claimed bind to a biological target, a recitation of a function is not the equivalent of a structure/function correlation. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to bind a biological target. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

Previously, claims were rejected under 102 based on the reference cited below. Since claims have been amended an updated rejection appears below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,3,32-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Bullesbach et al. (Chem Pept Proteins Proc 1982 pages 327-335, cited in IDS 8/7/08 as cite AD).

Bullesbach teach the preparation of the B-chain of an insulin peptide (Figure 2, page 328 last paragraph) in which cysteine residues are cross-linked. Since Bullesbach teach that the peptide was prepared it was necessarily present in a composition as recited in claims 32-33.

Although unclear, for purposes of examination the claims have been interpreted such that the peptides are cyclic. Since the location of the cyclic modification is unclear, any cyclic modification is interpreted as reading on the claims. Further, the claims have been interpreted such that the cyclic peptide must have one residue in common with the recited SEQ IDs and other modifications can occur at any other position. In the instant case Bullesbach specifically show a cross-link between amino acids (Figure 2). Further, the peptide of Bullesbach shares residues with SEQ ID NO:7 (for example Leu).

It is noted that claim 1 states that the peptide modulates an activity of the biological target and that residues are separated by a certain distance. Section 2112.01 of the MPEP states that products of identical chemical compositions can not have mutually exclusive properties. In the instant case, the peptide of Bullesbach meet the claim limitations so the peptide necessarily has the claimed activity absent evidence to the contrary.

Response to Arguments 102

Since the claims have been amended, a rejection adapted to the claims is recited above. Applicants arguments will be considered to the extent that they apply to the current rejection and claim set.

Applicants argue (pages 18-19) that none of sequences SEQ ID NO:1-3,7,8-10 represent the B-chain of proinsulin and that position 19 is outside the claimed range.

Applicant's arguments filed 2/8/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 18-19) that none of sequences SEQ ID NO:1-3,7,8-10 represent the B-chain of proinsulin, it is noted that the instant claims are not drawn to SEQ ID NO:1-3,7,8-10 but to modifications of SEQ ID NO:1-3,7,8-10. It is noted that SEQ ID NO:7, for example, is separate and distinct from modified SEQ ID NO:7. The specification (page 5 line 14) refers to at least two modifications. Page 14 of the specification refers to various modifications. It is noted that claim 1 and 3 refer to SEQ ID NO:7 which is a 31 amino acid sequence: PTPEMREKLCGHHFVRALVRVCGGPRWSTEA. The specification (Figure 3, and dependent claims 50-51) teach particular peptides that are apparently based on SEQ ID NO:7. The peptide identified as cINSL3a (see figure 3 and claim 50) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), positions 29-31 (deletion of TEA) if one were to interpret the modifications in relation to SEQ ID NO:7. Thus, there are modification outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. It would not be consistent with the specification to interpret positions 2 and 8, and positions 21 and 26 as in reference to SEQ ID NO:7. Further, the peptide identified as cINSL3b (see figure 3 and claim 51) includes modification at positions including position 1 (deletion of P), position 10 (change of C to S), position 12 (change of H to R), positions 29-31 (deletion of TEA) in relation to SEQ ID NO:7. Thus, there are at least 6 modifications outside of the recited range of positions 2 and 8, and 21 and 26 if one used SEQ ID NO:7 as the peptide basis of comparison. Although unclear, for purposes of examination the claims have been interpreted such that the peptides are cyclic. Since the location of the cyclic

modification is unclear, any cyclic modification is interpreted as reading on the claims. Further, the claims have been interpreted such that the cyclic peptide must have one residue in common with the recited SEQ IDs and other modifications can occur at any other position. In the instant case Bullesbach specifically show a cross-link between amino acids (Figure 2). Further, the peptide of Bullesbach shares residues with SEQ ID NO:7 (for example Leu).

Conclusion

Previously, claims 1,3,32-33 were rejected under 112 2nd, 112 written description, and 102. Since the claims have been amended the rejections have been updated to correspond to the instant claims. As such, applicants amendments have necessitated any new grounds of rejections.

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654